Epitomes

Important Advances in Clinical Medicine

Pediatrics

The Scientific Board of the California Medical Association presents the following inventory of items of progress in pediatrics. Each item, in the judgment of a panel of knowledgeable physicians, has recently become reasonably firmly established, both as to scientific fact and important clinical significance. The items are presented in simple epitome and an authoritative reference, both to the item itself and to the subject as a whole, is generally given for those who may be unfamiliar with a particular item. The purpose is to assist busy practitioners, students, research workers, or scholars to stay abreast of these items of progress in pediatrics that have recently achieved a substantial degree of authoritative acceptance, whether in their own field of special interest or another.

The items of progress listed below were selected by the Advisory Panel to the Section on Pediatrics of the California Medical Association and the summaries were prepared under its direction.

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Ribavirin and Respiratory Syncytial Virus Infections

RESPIRATORY SYNCYTIAL VIRUS (RSV) is the most frequent cause of hospital admissions of infants with respiratory tract disease. In previously healthy infants, the RSV infection subsides in three to seven days, and most infants recover without sequelae; some will have reactive airway disease with subsequent respiratory tract infections. Substantial morbidity and, infrequently, death may occur among infants with preexisting severe pulmonary or cardiac disease. Most severely affected infants have signs and symptoms of bronchiolitis or acute pneumonitis, or both, and clinically significant hypoxemia develops due to bronchiolar spasm or alveolar-capillary block, or both. A significant proportion of the sickest infants require ventilatory support. In those infants with severe bronchopulmonary dysplasia, severe cyanotic heart disease with increased pulmonary blood flow, and cellular immunodeficiency syndromes, the outcome may be uncertain.

RSV infection is generally limited to the respiratory tract epithelium; the pathogenesis of the disease probably is an extensive cellular pathologic disorder and acute host-mediated responses, including immunoglobulin (Ig) E-mediated activity. Ribavirin aerosol therapy, developed over the past decade, appears to ameliorate or diminish these pathologic events.

Ribavirin (Virazole) is a nucleoside analogue that is activated in host tissues to its phosphorylated form; antiviral activity results in the inhibition of viral RNA synthesis. Ribavirin aerosol therapy was pioneered in controlled studies among college students with acute influenza virus A infections and then extended to RSV infections among infants. Therapeutic efficacy has been shown among infants and children admitted to hospital with and without preexisting pulmonary and cardiac disease. Benefits occur without significant drug toxicity, and five-year follow-up evaluations show no effects of the aerosol therapy on the respiratory tract.

High concentrations of ribavirin are delivered in an aerosol by a small-particle aerosol generator through a mask, tent, or endotracheal tube over a 12- to 18-hour treatment period per day for three to five days or, in some cases, longer. The respiratory staff needs to give careful attention to drug precipitation in the respiratory equipment during therapy, especially among patients with endotracheal tubes in place.

In general, ribavirin therapy may be expected to control chronic infections among immunocompromised patients and to ameliorate infections among other treated inpatients. The most significant result of therapy is the relief of hypoxemia; this may be due to the control of the virus infection, an inhibition of IgE-mediated responses by ribavirin, or both. Ribavirin aerosol therapy may be indicated in infants and young children with RSV infection complicated by pneumonia, apnea, progressive bronchiolitis with hypoxemia, congenital heart disease, and chronic lung disease.

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Update on α-Fetoprotein Screening

SCREENING OF ALL PREGNANCIES for neural tube and other birth defects, using the maternal serum α-fetoprotein (AFP) level, is now a routine practice.

AFP produced by the fetal liver appears in the maternal serum in a measurable quantity by the 15th completed week and increases in concentration until term. Maternal serum AFP results are reported as multiples of the median value for a given gestational age and, as such, have provided a number of insights into conditions affecting a fetus or pregnancy.

The usefulness of maternal serum AFP screening is improved with accurate pregnancy dating and when raw values are adjusted for race, body weight, and the presence of insulin-dependent diabetes. The AFP levels can be raised or lowered in maternal serum by several conditions affecting fetal production or transplacental or amniotic diffusion. These conditions include multiple gestations; fetal demise; and structural fetal defects such as open spina bifida, gastroschisis, and omphalocele. It is necessary, therefore, to examine carefully the pregnancies of women having abnormal AFP values. This begins with ultrasonography to confirm the gestational age and the presence of a single fetus that is viable and has no structural defect. A woman with an abnormal

elevation unexplained by ultrasonography should have a specimen of amniotic fluid collected for karyotyping and AFP determination. If the AFP level is elevated, the acetylcholinesterase, an enzyme specific for neural tissue, is assayed. An elevation supports a diagnosis of open spina bifida.

The test should be done at a university or a referral laboratory with a large enough volume and experience to guarantee an accurate analysis and interpretation. The test is available in most states. California has pioneered and administered a statewide program that has screened more than 500,000 women. This program has proved to be cost-effective. The cost of care saved by termination or early treatment is about twice the cost of detection. Following this protocol, approximately 95% of anencephalic fetuses, 80% of those with open spina bifida, and many fetuses with ventral wall defects could be detected prenatally.

For several years women older than 35 years at term have been offered an amniocentesis for the prenatal detection of Down's syndrome. Because fetuses with the Down syndrome usually produce less AFP, low maternal serum AFP levels can now be used in women younger than 35 to identify an additional group of trisomic fetuses. The combination of maternal age and serum AFP levels in multiples of the median can be used to assign specific risk figures. Women with a risk equivalent to 35 years should be offered an amniocentesis. About 15% to 20% of cases of Down's syndrome are detectable by this method.

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Varicella Vaccine Update

THE FIRST REPORT OF VARICELLA VACCINE appeared in *The Lancet* a decade and a half ago. Since that time the vaccine has been licensed for use in Japan and in Europe. In the United States, the vaccine has been evaluated in thousands of normal children and in hundreds of normal adults and children with leukemia. Why has the vaccine not been licensed in this country? Varicella vaccine has been shown to confer good protection in healthy children and to modify or prevent disease in adults and in children with leukemia. In the latter groups, its use certainly reduces the morbidity that varicella is known to produce in these persons. In children with leukemia, there have been some reactions to the vaccine that are difficult to predict. In healthy children the vaccine is safe.

The main concern appears to be about the long-term effects of immunization: whether the vaccine will result in more or less zoster than in patients with natural infection. Studies in children with leukemia, however, do not suggest that there is increased risk, and, indeed, zoster may be less frequent in vaccinees. Another concern is whether the widespread use of the vaccine will result in a greater frequency of adult cases of varicella. This might occur if vaccine-induced immunity wanes or if the epidemiology of varicella is changed by reducing the opportunities for natural infection in those children who are not immunized. By combining the varicella vaccine with a vaccine that is given to virtually all children, such as the measles, mumps, and rubella vaccine, the latter concern can be assuaged. This combination has been shown to be safe and effective.

It is unlikely that we will have additional answers to these possible problems by more testing. A decision on licensure is probably at hand.

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Pediatric Physical Assessment of Sexual Abuse

CHILD SEXUAL ABUSE has been increasingly recognized in recent years. While physicians are sensitive to the psychological and social aspects of the medical evaluation, they need to be aware of the medical findings on physical examination associated with genital trauma and to understand the significance of sexually transmitted diseases in prepubescent children.

There is normal variation in the anatomy of the anogenital area of prepubescent children. Not all changes in the genital area are due to sexual abuse.

In general, the genital area of a prepubescent girl contains thin, fine structures that are scarred as a result of certain types of injuries. Not all forms of sexual abuse result in observable findings. Oral-genital contact and gentle fondling, for example, may result in no changes. External rubbing, also called vulvar coitus or dry intercourse, characteristically results in changes in the area of the posterior fourchette and occasionally hyperpigmentation of the labia majora. Actual penetration with either finger, penis, or foreign object will usually lead to disruptions in the configuration of the hymen. With a single isolated episode, the initial signs of trauma may heal within one to two weeks, and there may be minimal residual findings. With repeated episodes, the traumatized area may not have sufficient opportunity to heal, and greater changes are noted. In summary, the changes noted with repeated vaginal penetration are a reduced hymenal remnant; irregularities in the hymenal contour representing healed tears; rounding and thickening of the hymen; missing portions of the hymen; and a gaping, patulous introitus. There has been controversy concerning the size of the hymenal orifice as an indication of sexual abuse. In general, the orifice is 3 to 4 mm in girls younger than 5 years and up to 5 to 6 mm in girls between 5 and 10 years old. There is no consensus about these measurements, however, and the finding of an enlarged orifice without other changes may not be diagnostic of abuse.

Repeated penetration of the anus may lead to physical findings in only 50% of victims. Scarring, thickening, and hyperpigmentation of the perianal skin; a diminution in the number of rugae; a loss of tone; and a loss of subcutaneous supporting tissue may be present.

The presence of a sexually transmitted disease also supports the diagnosis of sexual abuse. These diseases include gonorrhea, *Chlamydia, Trichomonas,* syphilis, condylomata acuminata, and herpes simplex type 2. The presence of any of these diseases warrants further medical and psychosocial evaluation.

Referral centers with expertise in pediatric sexual abuse